UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Addr ss: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/351,149	07/12/99	THORPE	P 4001.002383

HM22/0313

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1619	16

DATE MAILED: 03/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/351,149	Thorpe et al
Examiner	**Group Art Unit**
Shahnam Sharareh	1619

☒ Responsive to communication(s) filed on *Dec 12, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-32 and 43-48* is/are pending in the applicat

Of the above, claim(s) *10-15, 20-23, and 44* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-9, 16-19, 24-32, 43, and 45-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *14*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Amendment filed on December 12, 2000 has been entered. Claims 1-32, 43-48 are pending. Applicant's election of amino phospholipid targeting agent, antibody or fragment thereof, a coagulant, and a second anti-cancer agent is acknowledged. Claims 1-9, 16-19, 24-32, 43 ~~44~~ 45-48 read on the elected species. Claims 10-15, 20-23, 44 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species. Applicant's assertion that claims 10-5, 20-23 and 44 are only drawn to initially non-elected "species", the treatment of which is governed by 37 CFR 1.114(a) is noted. Nevertheless, as set forth in Paper No. 8 the instant claims are drawn in Markush format and are directed to patentably distinct species.

In the event that the Markush-type claims are not found to be allowable, the examination of the claims presented will be limited to the Markush-type claims to the extent that they read on the elected species and claims directed solely to the elected species. The claims directed solely to the non-elected species will be held withdrawn from consideration. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case.

2. Clarification of previous ruling of the priority date is made. The effective priority date used for the examination of the instant application is July 13, 1998.

Response to Arguments

3. Applicant's arguments with respect to the rejection of claims 1-9, 16-19, 24-32, 43 under 35 U.S.C. 112, second paragraph, as being indefinite have been found persuasive. This rejection is withdrawn.

4. Applicant's arguments with respect to the rejection of claim 43 under 35 U.S.C. 112, second paragraph, has been fully considered. In view of the newly added claims and the arguments, Examiner now views "in combination" to encompass "a kit". This rejection is now moot.

5. Applicant's arguments with respect to the rejection of claims 1-9, 16-19, 24-32, 43 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-49 of U.S. Patent No. 6,036,955, claims 40-61 of U.S. Patent No. 6,051,230 have been fully considered. Applicant argues that the claims of the cited patents are not directed to a kits comprising a targeting agent-therapeutic agent construct that binds to an aminophospholipid. Accordingly, this rejection is withdrawn.

6. Applicant's arguments with respect to the rejection of claims 1-9, 16-19, 24-32, 43 under 35 U.S.C. 103(a) as being unpatentable over Huang et al, *Science* 275:547-550,1997 in view of Martin US Patent 6,043,094 have been fully considered and are found persuasive. This rejection is withdrawn.

7. Applicant's arguments with respect to the rejection of claims 1-9, 16-19, 24-32, 43 under 35 U.S.C. 103(a) as being unpatentable over Gimbrone et al US Patent 5,632,991 in view of Huang et al *Science* 275:547-550,1997 have been fully considered and are found persuasive. This rejection is withdrawn. Applicant's arguments with respect to the rejection of claims 1-9, 16-19, 24-32, 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gimbrone et al US Patent 5,632,991 in view of Dvorak et al, *Cancer cells*, 1991: 3(3); 77-85 have been fully considered and are found persuasive. This rejection is withdrawn.

Applicant's remarks with respect to the prosecution of the co pending application Serial No. 09/351,457 has been noted. The prosecution of this application is independent of its co pending counter part.

New Grounds of rejection

8. Claims 1-9, 16-19, 24-32, 43, 45-48 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "a second anti cancer agent" in claim 1 is vague. It is not clear to what second anticancer agent is applicant referring. The recitation of "a second anti cancer agent" lacks antacedent basis.

9. Claims 1-9, 16-19, 24-32, 43, 45-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blankenberg et al US patent 6,197,278 in view of Haung et al Science 275: 547 - 550 1997, and further in view of WO 98/29453('453) (IDS 1/24/2000), Fishman et al (IDS 2/14/2000).

Blankenberg et al disclose a methods of imaging cell death in cancer cells, using radiolabled annexin (abstract). Annexin is a peptide with high affinity to anionic phospholipid surface of the cell membrane. Blankenberg teaches targeting radio labeled annexin V directed to a selected organ for any desired condition such as cancer (col 9 lines 50-65, col 12 lines 33-61, col 20 lines 41-55). Blankenberg doesn't teach the use of a second anti-cancer agent for therapeutic or diagnostic purposes.

The teachings of Huang are discussed previously. Huang et al disclose methods of occluding tumor vasculature in solid tumors of mice by targeting the cell surface domain of tumor vascular endothelial cells with a bispecific antibody-tissue factor conjugate (abstract, page 549). Huang et al specifically teach that administration of a drug acting on the tumor cells and selective blood coagulation of tumor vasculature can improve efficacy of antivascular therapy of solid tumors (page 549, 3rd col). Huang, however, does not specifically teach targeting of aminophospholipids.

'453 patent teaches peptide drugs with specific affinity towards phosphatidylserine. The drugs disclosed in '453 are used to treat or prevent immunological disorders involving blood coagulation. '453 doesn't teach therapeutic construct directed to solid tumors (abstract)

Fishman discloses anti-phospholipid antibodies directed to melanoma cells and other the cancer cells having over expressed outer membrane phophatidilserine (abstract). Fishmann teaches the potential use of autoantibodies in diagnostic and therapeutic area (abstract). Fishmann also teaches the use of antiphospholipid for various types of cancer cells exhibiting

phophatidylserine on the outer cell membrane such as squamous cell carcinoma of the skin (page 903).

Although Blackenberg does not teach the use of a second anti-cancer agent in their imaging or therapeutic methods, it would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Blackenberg, and Haung to enhance the antivascular therapy of a solid tumor of interest, because Blackenberg suggests that his methods can be used for both therapeutic and imaging purposes, and Haung suggests that specific targeting of the tumor cell surface markers with bispecific antibodies such as those directed to MHC class II can significantly improve the efficacy of coaguligand therapy. Fishmann and WO '453 complement the teachings of Blackenberg and Haung because they show the general state of art form preparing peptide drugs and autoantibodies directed to aminophospholipids, thus, preparing such conjugates in combination or alone would have been obvious. Finally, preparing a convenient therapeutic kit for a clinical setting containing the essential components of such therapy would have been well within purview of an ordinary practitioner and thus obvious at the time of invention.

10. Claims 1-9, 16-19, 24-32, 43-48 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-10 of copending Application No. 09/351,457. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common

subject matter, as follows: both sets of claims are directed to methods and products directed to aminophospholipid targeting and cancer treatment.

Specification

11. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Additionally, as set forth in MPEP section 608.01, an application for a patent when filed may incorporate "essential material" by reference to (1) a U.S. patent or (2) a pending U.S. application. "Essential material" is defined as that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). In any application which is to issue as a U.S. patent, essential material may not be incorporated by reference to ...., (3) a U.S. patent or application which itself incorporates "essential material" by reference, ...See In re Fouche , 439 F.2d 1237, 169 USPQ 429 (CCPA 1971). Accordingly, the description of numerous Patented and literature publications through out the specification can not be incorporated, because they themselves contains subject matter that is incorporated by reference from another publication.

Conclusion

9. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash can be reached on 703-308-2328. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

ss 3/8/2001

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